UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/668,508	09/22/2000	Henry E. Young	1304-1-019CIP	1973

7590 10/19/2004

David A Jackson Esq
Klauber & Jackson
411 Hackensack Avenue
Hackensack, NJ 07601

EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/668,508	YOUNG ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Request for Continued Examination (RCE), filed 4/5/04, is proper and has been entered. Applicants' Amendment and Response, filed 8/27/04, has been entered. Claims 14 and 15 have been amended. Claims 14-17 are pending and under current examination.

Claim Objections

The prior objection of claim 15 is withdrawn in view of amendment to the claim.

Information Disclosure Statement

Applicants' Information Disclosure Statement, filed July 3, 2003, has been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 is unclear because it fails to recite that the cell is isolated. This encompasses a cell *in vivo*. Thus, it is unclear if Applicants are claiming an isolated cell or an animal comprising the cell. Recitation of "isolated" would obviate this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Capecchi *et al.* [**Scientific American**, 270(3):34-41 (1994)].

The claims are directed to pluripotent embryonic-like stem cells, derived from non-embryonic or postnatal animal cells or tissue, capable of self-renewal and differentiation to cells of any of endodermal, ectodermal, and mesodermal lineages, genetically engineered to express a gene or protein of interest. Note that claim 16 is a product-by-process claim, and methods of producing the same. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether

the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Further, see MPEP §2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

Capecchi teach the inactivation of target genes by homolgous recombination, and the insertion of a *neo* resistance gene, which serves as a positive selection marker in mouse ES cells. See Figure, p. 36. They teach that the ES cells are then cultured and grown into surrogate mothers to generate chimeric mice. See p. 38, Figure. Note that the claimed cells are not distinguished from those taught by Capecchi. Capecchi fulfills the limitations of the claims (the differentiation to cells of any endodermal, ectodermal, mesodermal lineage) by showing the generation of mice; further, the methods of producing the genetically engineered cells are also anticipated by Capecchi because they teach transfection of pluripotent embryonic-

like stem cells. The claims do not distinguish the instantly claimed cells from those taught in the art. Accordingly, Capecchi anticipate the claims.

Claims 14-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Povey *et al.* [**Blood**, 92(11):4080-4089 (1998)]

Povey teach the transfection of pluripotent human hematopoietic stem cells using a retroviral vector. They teach that hematopoietic stem cells are capable of multilineage differentiation and self-renewal (see *Abstract*). Particularly, they teach that the cells were transduced using a viral producing cell line that expresses the membrane-bound form of human stem cell factor (see *Abstract* and *Methods and Materials*). As *supra*, claims 16 and 17 are product-by-process claims. Further, as the instant claims fail to be distinguished from the cells taught by the art, Povey anticipates the claims.

Claims 14-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Verma *et al.* [**Gene Therapy**, 5:692-699 (1998)].

Verma teach the transfection of hematopoietic progenitor cells using a CMV-CAT reporter plasmid. See *Abstract*. They teach that the hematopoietic progenitor cells are isolated from bone marrow, peripheral and umbilical cord blood and are able to differentiate into cells of the hematopoietic lineage. See p. 692, 1st column. Further, it is reiterated that the claims as written only require that the cells be

capable of differentiation to cells of any of endodermal, ectodermal and mesodermal lineages. Thus, Verma fulfills this limitation and anticipates the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The prior rejection of claims 14-17 under 35 U.S.C. 103(a) as being unpatentable over Pittenger *et al.* [**Science**, 284:143-147, 2 April 1999] in view of

Sambrook *et al.* [**Molecular Cloning**, Book 3, 1989] is *maintained* for reasons of record.

Note that claims 16 and 17 are product-by-process claims. See supra. In the prior Office action, the Examiner stated that the mesenchmyal stem cells taught by Pittenger would be pluripotent stem cells, as required by the claims. Applicants argue that the teaching which shows differentiation into one of the endodermal, ectodermal, or mesodermal lineages, does not anticipate the stem cells as presently claimed, because the claimed stem cells can differentiate into any of endodermal, ectodermal and mesodermal lineages. Particularly, Applicants point to the specification to show that extensive teaching and specific examples define and characterize the novel pluripotent embryonic-like stem cells as distinct from any other pluripotent stem cells known in the art. Applicants argue that the claims as amended are not obvious nor anticipated by the cited art because the art does not show differentiation into all three lineages, the art does not make obvious or anticipate the instant claims. Applicants point to the specification for teaching and specific examples that define the novel pluripotent embryonic-like stem cells as distinct. Applicants argue that the claims now require that the claimed cells be capable of differentiating into all three of the endodermal, ectodermal and mesodermal lineages, and thus, because Pittenger teaches mesenchymal stem cells which can only differentiate into a single lineage, Pittenger do not anticipate the stem cells of Applicants. See p. 4 of the Response.

This is not persuasive. The claims as written state that the cells can differentiate into any of the three (endodermal, ectodermal and mesodermal) lineages. Thus, as amended, the claims are written in the alternative, and do not require differentiation into all three lineages. As the cells from Pittenger teach that they can differentiate into multiple mesenchymal lineages, they fulfill the requirements of the claims. Furthermore, Applicants have failed to provide any teachings or evidence to distinguish the instantly claimed cells, and those as taught by the art. For example, the requirements for the cells to be capable of self-renewal and capable of differentiation of the cells to any of the three embryonic germ layers fails are fulfilled by the cited art. Pittenger teach human mesenchymal stem cells which are capable of differentiation into multiple mesenchymal lineages. As such, Pittenger teach pluripotent stem cells, as required by the claims.

Pittenger teach human mesenchymal stem cells isolated from adult bone marrow which are found to differentiate into multiple mesenchymal lineages *in vitro* [see p. 143, 2nd column, 1st full paragraph]. Pittenger teach that these mesenchymal cells were characterized by their ability to proliferate in culture [see Figure 1]. Pittenger teach that the differentiation potential of the mesenchymal stem cells was tested by specific differentiation in adipogenic differentiation, chondrogenic differentiation and osteogenic differentiation under specific conditions [see pp. 144-145]. They differ from the claimed invention in that they do not teach

transfecting the pluripotent embryonic stem-like stem cells with a DNA construct comprising at least one of a marker gene or a gene of interest.

However, prior to the time of the claimed invention, Sambrook teach methods of transfecting mammalian cells with any gene of interest [see 16.33-16.38]. Accordingly, in view of the combined teachings of Pittenger and Sambrook, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to use the mesenchymal stem cells, as taught by Pittenger and transfect them with any DNA of interest, with a reasonable expectation of success. One of skill in the art would have been sufficiently motivated to make such a modification, as expression of proteins in mammalian cells can provide different purposes, as described by Sambrook on p. 16.3, such as for the expression of large amounts of protein of biological interest, or to study the biosynthesis and intracellular transport of proteins following their expression in various cell types.

Thus the claimed invention as a whole was clearly *prima facie* obvious at the time the claimed invention was made especially in the absence of sufficient, clear and convincing evidence to the contrary.

Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shamblott (cited in the prior Office action, **PNAS**, 95:13726-13731, 1998) when taken with Sambrook *et al.* [cited in the prior Office action, **Molecular Cloning**, Book 3, 1989].

The claims are directed to a pluripotent embryonic-like stem cell, derived from non-embryonic or postnatal animal cells or tissues, capable of self-renewal and capable of differentiation to cells of any of endodermal, ectodermal and mesodermal lineages, genetically engineered to express a gene or protein of interest, wherein the cell is a human cell and methods of producing the same.

Note that claims 16 and 17 are product-by-process claims. See *supra* and the prior Office action. Shamblott *et al.* teach the generation of human pluripotent stem cells from gonadal ridges and mesenteries containing primordial germ cells [PGCs] and teach that embryoid bodies collected from these cultures revealed a wide variety of differentiated cell types, including derivatives of all three embryonic germ layers [see *Abstract*]. In particular, Shamblott *et al.* teach that gonadal ridges and mesenteries of 5 to 9 week old human fetuses and cells initially cultured on a layer of mouse STO fibroblast feeder layer. The cells formed embryoid bodies, which were collected and analyzed immunohistochemically [see pp. 13726-13727, *Materials & Methods*]. It was found that the embryoid bodies demonstrated derivatives of the three embryonic germ layers [see p. 13729, 2nd column and Table 1]. Note that Shamblott teach the pluripotent embryonic-like stem cells because the claims do not provide any requisite characteristics (*e.g.*, specific markers, etc.) of the claimed embryonic-like stem cells such that they would be distinguished from the cells taught by Shamblott. Although the claims recite that the embryonic-like stem cells are "derived from non-embryonic or postnatal animal cells or tissue," however,

this recitation does not differentiate them from the cells as taught by Shamblott. Further, the method claim has been included in this rejection because the cells as instantly claimed are not distinguishable from those taught in the art. The cells as taught by Shamblott fulfill the requirements of the claims because they are capable of differentiation to cells of any of endodermal, ectodermal and mesodermal lineages, and are capable of self-renewal.

Shamblott do not teach the transfection of the pluripotent stem cells to produce a genetically engineered pluripotent stem cell. However, prior to the time of the claimed invention, Sambrook teach methods of transfecting mammalian cells with any gene of interest [see 16.33-16.38]. Accordingly, in view of the combined teachings of Pittenger and Sambrook, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to use the mesenchymal stem cells, as taught by Pittenger and transfect them with any DNA of interest, with a reasonable expectation of success. One of skill in the art would have been sufficiently motivated to make such a modification, as expression of proteins in mammalian cells can provide different purposes, as described by Sambrook on p. 16.3, such as for the expression of large amounts of protein of biological interest, or to study the biosynthesis and intracellular transport of proteins following their expression in various cell types.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson [Reference BR on Applicants' IDS, filed 7/3/03, PNAS USA, 92:7844-8 (1995)] when taken with Sambrook *et al.* [cited in the prior Office action, **Molecular Cloning**, Book 3, 1989].

As stated previously, claims 16 and 17 are product-by-process claims. Thomson teach the isolation of ES cells from the rhesus monkey. See p. 7844, *Materials and Methods*, col. 2. The cells are capable of maintaining an undifferentiated state and proliferate indefinitely, and have the potential to differentiate into derivatives of all three embryonic germ layers. They teach that the cells differentiated into cells of endoderm, mesoderm and ectoderm. See *Abstract* and p. 7846, col. 1-2, bridging ¶. Note that the claims fail to distinguish the claimed cells from the cells taught by Thomson. Thus, the method claim has been included in the rejection because the cells used in the method are not distinguished from those taught by Thomson. Thomson do not teach that the ES cells are genetically engineered to express a gene or protein of interest.

However, prior to the time of the claimed invention, Sambrook teach methods of transfecting mammalian cells with any gene of interest [see 16.33-16.38]. Accordingly, in view of the combined teachings of Pittenger and Sambrook, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to use the mesenchymal stem cells, as taught by Pittenger and

transfect them with any DNA of interest, with a reasonable expectation of success. One of skill in the art would have been sufficiently motivated to make such a modification, as expression of proteins in mammalian cells can provide different purposes, as described by Sambrook on p. 16.3, such as for the expression of large amounts of protein of biological interest, or to study the biosynthesis and intracellular transport of proteins following their expression in various cell types.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Amy Nelson, Acting SPE of Art Unit 1632, at (571) 272-0804. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

tnt
Thaian N. Ton
Patent Examiner
Group 1632

Joe Woitach
- AU1632